General

Guideline Title

ACR Appropriateness Criteria® spinal bone metastases.

Bibliographic Source(s)

Lo SS, Lutz ST, Chang EL, Galanopoulos N, Howell DD, Kim EY, Konski AA, Pandit-Taskar ND, Rose PS, Ryu S, Silverman LN, Sloan AE, Van Poznak C, Expert Panel on Radiation Oncology-Bone Metastases. ACR Appropriateness CriteriaÂ® spinal bone metastases. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 13 p. [37 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Janjan NA, Lutz ST, Bedwinek JM, Hartsell WF, Ng A, Pieters RS Jr, Ratanatharathorn V, Silberstein EB, Taub RJ, Yasko AW, Expert Panel on Radiation Oncology--Bone Metastases. ACR Appropriateness Criteria® bone metastasis. [online publication]. Reston (VA): American College of Radiology (ACR); 2008. 26 p.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Spinal Bone Metastases

Variant 1: 55-year-old patient with lung cancer with KPS 70 and a history of prior EBRT for a Pancoast tumor, including vertebral levels C7-T4. He received three lines of systemic therapy prior to presenting with symptomatic vertebral metastases (pain scale 6 out of 10) with paraspinous soft-tissue extension from T6-10 with spinal cord compression and mild weakness. Diffuse metastatic disease is noted on bone scan, and multiple small liver metastases are evident on CT of abdomen.

Treatment	Rating	Comments
Hospice after EBRT	8	
EBRT alone	8	
Direct hospice placement	5	Given the expected poor prognosis, direct hospice placement may be appropriate if pain can be adequately controlled by pharmacologic means.
Chemotherapy	1,2,3	After progression after third line therapy there are insufficient

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

Treatment	Rating	Comments
		data to suggest benefit from additional lines of systemic treatment. Consideration for participation in clinical trials may be given for select individuals.
Chemotherapy and OI and EBRT	2	
Chemotherapy alone	2	
Systemic radiopharmaceuticals	2	
Surgical intervention	2	
Chemotherapy and OI	2	
Radiation Therapy Dose		
8 Gy/1 fraction	8	
20 Gy/5 fractions	8	
30 Gy/10 fractions	8	
35 Gy/14 fractions	3	
40 Gy/20 fractions	2	
Treatment Planning		
CT simulation	8	
Fluoroscopic simulation	8	
Clinical simulation	3	
Posterior field only	7	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used.
Anterior-posterior fields	7	
Posterior obliques	7	
SBRT	2	
IMRT	2	
Proton therapy to the bone metastasis	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: 55-year-old woman with ER positive/PR positive and HER2 negative breast cancer, and new metastases with symptomatic (pain scale 7 out of 10) vertebral metastases at T12, L1, and L2, with no compression fracture or canal involvement. In addition, she has diffuse asymptomatic metastases on bone scan, rising CEA and no prior EBRT to spine. KPS 80, with no visceral tumor burden. No prior HT.

Treatment	Rating	Comments
HT and EBRT	8	
HT and OI and EBRT	8	
Chemotherapy and HT and EBRT	5	
Chemotherapy and HT and OI and EBRT	5	

Treatment	Rating	Comments
Chemotherapy and EBRT	3	
HT alone	3	
Chemotherapy alone	3	
EBRT alone	3	
Systemic radiopharmaceuticals alone	2	
Surgical intervention	2	
Direct hospice placement	2	
Hospice after EBRT	2	
Radiation Therapy Dose		
8 Gy/1 fraction	8	
20 Gy/5 fractions	8	
30 Gy/10 fractions	8	
35 Gy/14 fractions	5	
40 Gy/20 fractions	3	
Treatment Planning		
CT simulation	8	
Fluoroscopic simulation	8	
Clinical simulation	3	
Posterior field only	7	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used.
Anterior-posterior fields	8	
Posterior obliques	7	This technique helps preserve the skin if surgical intervention of the spine come into play in later course of disease, but it is only deemed appropriate if the kidneys can be spared.
SBRT	3	
IMRT	2	
Proton therapy to the bone metastasis	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: 54-year-old man presents with newly diagnosed multiple myeloma. He develops mild bilateral lower-extremity weakness (motor power 5 minus out of 5) from an epidural spinal cord compression at T7 seen on MRI, associated with severe pain (scale 8 of 10). KPS 80. Skeletal survey reveals several other sites of asymptomatic lytic metastases.

Treatment	Rating	Comments
Steroid therapy and EBRT, followed by OI and chemotherapy	8	EBRT sequentially with systemic therapy.
Steroid therapy, EBRT, and chemotherapy	8	EBRT concurrently with systemic therapy.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Treatment	Rating	Comments
chemotherapy		
Steroid therapy and EBRT, followed by OI	6	
Steroid therapy and EBRT	6	
Steroid therapy and OI and chemotherapy	3	
Steroid therapy and chemotherapy	3	
Steroid therapy and OI	3	
EBRT alone	3	
Steroid therapy alone	2	
OI alone	2	
Hospice after EBRT	2	Life expectancy would be expected to be >6 months.
Observation	1	
Systemic radiopharmaceuticals alone	1	
Direct hospice placement	1	Life expectancy without treatment still could be >6 months, although paraplegia would be expected to occur.
Radiation Therapy Dose		
8 Gy/1 fraction	6	
20 Gy/5 fractions	8	
30 Gy/10 fractions	8	
35 Gy/14 fractions	6	
40 Gy/20 fractions	5	
Treatment Planning		
CT simulation	8	
Fluoroscopic simulation	8	
Clinical stimulation	5	
Posterior field only	6	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used.
Anterior-posterior fields	7	
Posterior obliques	7	This technique can help preserve skin if spinal surgery comes into play in later course of disease but it will result in higher lung doses.
SBRT	2	
IMRT	2	
Proton therapy to the bone metastasis	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: 72-year-old man with non-small-cell lung cancer, 2 years status post right upper lobectomy with a KPS 80. He received previous RT to the T5-T8 spine 10 months ago to 30 Gy in 10 fractions. He also received two lines of systemic chemotherapy. Now he presents with debilitating

pain (pain scale 8 out of 10) from recurrent disease at T7 with no canal involvement. Diffuse asymptomatic bone metastasis, stable on bone scan with no visceral metastases.

Treatment	Rating	Comments
Surgical intervention alone	6	Surgery may be considered if the adjacent, irradiated bone appeared stable and the patient's life expectancy was >3 to 6 months.
EBRT alone	6	EBRT in the form of SBRT or IMRT if they are available and sustained positioning is achievable for the patient.
Surgical intervention and EBRT	6	If life expectancy >3 to 6 months; EBRT in the form of SBRT if they are available and sustained positioning is achievable for the patient. See comments about surgery in text.
Surgical intervention and EBRT and systemic radiopharmaceuticals	5	If life expectancy >3 to 6 months; EBRT in the form of SBRT if they are available and sustained positioning is achievable for the patient.
Surgical intervention and systemic radiopharmaceuticals	5	
Hospice after treatment (surgery or SBRT) of the spine	5	
Systemic radiopharmaceuticals alone	3	
Direct hospice placement	3	
Chemotherapy	4	Third line chemotherapy with erlotinib may be considered for individuals who have a good performance status and who have not had prior exposure to erlotinib or gefitinib. There is insufficient data addressing use of additional cytotoxic drugs; considerations may be given to clinical trials and best supportive care.
OI alone	3	
SBRT Dose		
12-18 Gy/1 fraction	7	Spinal cord tolerance permitting.
21-27 Gy/3 fractions	7	Spinal cord tolerance permitting.
20-30 Gy/5 fractions	7	Spinal cord tolerance permitting.
Treatment Planning		
CT simulation	9	CT simulation is mandatory if SBRT is offered since sophisticated dose planning is required.
Fluoroscopic simulation	3	
Clinical simulation	3	
Posterior field only	3	
Anterior-posterior fields	3	
Posterior obliques	3	
SBRT	7	Treatment planning technique depends on treatment device used.
IMRT	6	
Proton therapy to the bone metastasis	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 5: 56-year-old postmenopausal woman with ER positive/PR positive and HER2 negative breast cancer and a KPS of 90. At diagnosis, she developed a painful, solitary, biopsy-proven bone metastasis at T4 level with no canal involvement or compression fracture/spinal instability and no other sites of metastasis.

Treatment	Rating	Comments
HT and EBRT	8	
HT and OI and EBRT	8	
Chemotherapy and HT and EBRT	5	
Chemotherapy and HT and OI and EBRT	5	
HT and OI	4	
HT alone	4	
Chemotherapy alone	3	
Surgical intervention	3	
Systemic radiopharmaceuticals alone	2	
OI alone	2	
Direct hospice placement	1	Life expectancy would be expected to be >6 months.
Hospice after EBRT	1	Life expectancy would be expected to be >6 months.
Radiation Therapy Dose		
8 Gy/1 fraction	8	
20 Gy/5 fractions	8	
30 Gy/10 fractions	8	
35 Gy/14 fractions	5	There may be a potential survival benefit to aggressive local therapy of oligometastasis but more data is needed to better define the role of this approach.
40 Gy/20 fractions	5	There may be a potential survival benefit to aggressive local therapy of oligometastasis but more data is needed to better define the role of this approach.
Treatment Planning		
CT simulation	8	CT simulation is mandatory if SBRT is offered since sophisticated dose planning is required.
Fluoroscopic simulation	8	
Clinical simulation	5	
Posterior field only	6	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used. The skin dose is a concern for this patient who is expected to have more favorable prognosis as spinal surgery may be needed in later course of her disease.
Anterior-posterior fields	7	
Posterior obliques	7	This technique can help preserve skin if spinal surgery comes into play in later course disease but it will result in higher lung doses.
3D-CRT	7,8,9	There may be a potential survival benefit to aggressive local therapy of oligometastasis but more data is needed to better define the role of

Treatment	Rating	SBRT in this type of clinical scenario. Comments
IMRT	2	
Proton therapy to the bone metastasis	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 6: 45-year-old woman with metastatic renal cell carcinoma, involving her lungs and T9, and a KPS of 90, received sunitinib and developed progressive single spinal metastasis at T9 with no canal involvement or compression fracture. Her other extraspinal metastases in the lungs and right adrenal were stable.

Treatment	Rating	Comments
Systemic therapy and EBRT	7	
Systemic therapy and EBRT and OI	7	
Systemic therapy and OI	5	
Systemic therapy alone	4	
EBRT alone	3	
Surgical intervention	3	
OI alone	3	
Systemic radiopharmaceuticals alone	2	
Direct hospice placement	2	
Hospice after EBRT	2	
Radiation Therapy Dose		
8 Gy/1 fraction	5	
20 Gy/5 fractions	7	
30 Gy/10 fractions	7	
35 Gy/14 fractions	7	
40 Gy/20 fractions	5	
20-30 Gy/5 fractions (SBRT)	7	Spinal cord tolerance permitting.
18-27 Gy/3 fractions (SBRT)	7	Spinal cord tolerance permitting.
15-24 Gy/1 fraction (SBRT)	7	Spinal cord tolerance permitting.
Treatment Planning		
CT simulation	9	CT simulation is mandatory if SBRT is offered since sophisticated dose planning is required.
Fluoroscopic simulation	7	
Clinical simulation	5	
Posterior field only	6	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used.
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Treatment	Rating	Comments
Anterior-posterior fields	7	
Posterior obliques	7	This technique can help preserve skin if spinal surgery comes into play in later course of disease but it will result in higher lung doses.
SBRT	7	Since renal cell carcinoma is radioresistant histology, there may be a benefit to using SBRT, which delivers ablative doses of radiation to the spinal metastatic lesion.
IMRT	4	
Proton therapy to the bone metastasis	1	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

The axial skeleton is a common site of involvement in patients with bone metastases. Apart from pain, hypercalcemia, and pathologic fracture, progressive tumor can result in neurologic deterioration caused by spinal cord compression or cauda equina involvement. The treatment of spinal bone metastases depends on many factors including histology, site of disease, extent of epidural disease, extent of metastases elsewhere, and neurologic status. Ideally, patients with spinal bone metastases are evaluated by an interdisciplinary team including a combination of radiation oncologists, medical oncologists, spine surgeons, pain medicine specialists, interventional radiologists, psychiatrists, and palliative care professionals. Treatment recommendations must weigh the risk-benefit profile of radiation therapy (RT) for the particular individual's circumstance, including neurologic status, performance status, extent of spinal disease, stability of the spine, extra-spinal disease status, and life expectancy. Patients with spinal instability should be evaluated for surgical intervention. Research studies are needed that evaluate the combination or sequencing of localized therapies such as surgery and external beam radiotherapy (EBRT) with systemic therapies including chemotherapy, hormonal therapy (HT), osteoclast inhibitors (OI), and radiopharmaceuticals.

Under current practice, systemic chemotherapy and/or HT and OI are frequently administered when asymptomatic bone metastases are first diagnosed. EBRT is usually delayed until the metastatic disease progresses and causes significant pain or creates a risk for pathological fracture or spinal cord compression. The use of radiopharmaceuticals is generally considered in a small fraction of patients with persistent multifocal sites of pain or recurrence of pain in a previously irradiated site.

Stereotactic body radiation therapy (SBRT) is an emerging therapy for spinal metastasis as primary treatment, postoperative treatment, or salvage treatment after prior EBRT or spinal cord compression. Preliminary results based on retrospective studies and a small number of prospective studies appear to be promising, but the follow-up intervals for most studies are short and the reported endpoints are not uniform, rendering comparison with other conventional therapies difficult. A limited number of prospective studies and clinical trials show promising results. SBRT's roles in the management of spinal oligometastasis, radioresistant spinal metastasis, and previously irradiated but progressive spinal metastasis are emerging, but more research is needed to validate the findings from retrospective studies. Logistically, the treatment planning and delivery processes require much more time and resources.

Epidural spinal cord compression represents a special situation for treating spinal metastasis and is an oncologic emergency. The key goal of the treatment is prompt decompression of the spinal cord in order to prevent further deterioration of neurologic function or to reverse the neurologic deficits. This can be accomplished by surgical decompression or EBRT. For most solid tumors, except radio- and chemo-sensitive tumors such as germ cell tumors and small-cell carcinomas, surgical decompression followed by EBRT has been demonstrated to yield superior functional outcomes compared to EBRT alone. For patients who have poor performance status or are not suitable for surgery, EBRT is regarded as a reasonable option, although there is some debate as to optimal dose schedules and fractionation. Hematologic tumors such as lymphoma and plasma cell tumors/myeloma are radiosensitive, and EBRT alone is effective decompressing the spinal cord. SBRT has been used to decompress spinal cord compression, but data in the literature are limited. More research is needed to define its role in managing spinal cord compression.

Variant 1 Discussion

This is a case of spinal cord compromise involving a region that has not been previously irradiated. This patient is expected to have very poor prognosis, and local palliative EBRT to prevent lower-extremity paralysis before referral for hospice care is regarded as the most appropriate treatment plan. Medications to aid symptom control may include steroids and analgesics. Moderate- to high-dose steroids are typically used in managing spinal cord involvement. Hospice placement after EBRT is favored to avoid the logistic difficulties of coming to the radiation center for EBRT, although some hospices accommodate palliative EBRT.

Due to the spinal cord compression and the bulk of disease with paraspinous involvement, computed tomography (CT) simulation and EBRT are recommended, ranging from a single 8 Gy fraction to 30 Gy in 10 fractions. Given the poor prognosis, a single dose of 8 Gy is deemed as appropriate as 20 Gy in 5 fractions and 30 Gy in 10 fractions, and longer fractionation regimens such as 35 Gy in 14 fractions and 40 Gy in 20 fractions are deemed not to be appropriate since long term toxicities are not an active concern in this case. Fluoroscopic simulation is regarded as a reasonable alternative. Clinical simulation, defined as setting up of a patient at the treatment machine without kilovoltage films, is usually not preferred. Common EBRT field arrangements, anterior/posterior (AP/PA), PA and posterior obliques alone, are considered appropriate. Highly conformal approaches like SBRT, intensity-modulated radiation therapy (IMRT), and protons are considered inappropriate given the expected poor prognosis, the need for prompt treatment, the numerous levels involved, and the limited data on these approaches. Surgical intervention is not considered appropriate due to the expected poor prognosis, the multiple vertebral levels involved, and the limited life expectancy. There are concerns regarding the futility of administering further chemotherapy, given the prior treatment history and the extent of tumor burden, although the patient may be considered for an experimental protocol if it is available and the patient is deemed eligible (see Variant 1 above).

Variant 2 Discussion

There is a localized symptomatic region of bone metastases. This patient has a fairly good performance status and vertebral involvement. She has incurable disease, and the goals of care are palliative. The use of EBRT with analgesics, initiation of HT, and OI is regarded as the most appropriate treatment. HT, like localized RT, incurs limited morbidity while treating symptomatic disease and limiting consequential disease progression. The use of RT to control pain and tumor burden constitutes a skeletal-related event (SRE). This scenario warrants the use of an OI to further reduce the risk of additional SREs. In light of the slight risk of jaw osteonecrosis associated with OI administration, a pretreatment dental evaluation to assess dentition and potential risk prior to OI use might be necessary. The addition of chemotherapy after EBRT and HT (given sequentially), with or without OI is regarded as less appropriate due to the considerable morbidity of chemotherapy, limited survival benefit, and quality of life during the course of chemotherapy given the lack of visceral tumor burden and the expected symptom control with EBRT, HT, and OI. For this estrogen receptor (ER) positive and progesterone receptor (PR) positive tumor, the use of chemotherapy (with or without OI) and EBRT without HT is deemed inappropriate. Systemic radiopharmaceuticals and surgical intervention are regarded as the least appropriate. For this clinical situation, life expectancy may potentially be measured in years; hence hospice is not typically an appropriate next step.

HT and OI with analgesics may be considered options for the initial intervention. However, EBRT offers the patient an excellent likelihood of expedient pain control and can be used in conjunction with HT, OI, and analgesics and is a favored approach due to the magnitude of her pain. In this symptomatic spine lesion where disease progression under systemic therapy alone could incur the risk of spinal cord compression, the benefit of adding EBRT to any systemic regimen is emphasized. If EBRT is not administered to the spine at this time, then very close monitoring of the patient would be required to monitor for pain as well as early symptoms of spinal cord compression.

The RT dose fractionation prescribed for spinal metastases varies from those for long bones. Fractionation schedules ranging from a single 8 Gy fraction to 35 Gy in 14 fractions are all considered appropriate, while 40 Gy in 20 fractions is considered less appropriate due to the protracted length of therapy. CT simulation, to accurately include the involved vertebrae and account for body habitus in EBRT dose calculation is most desirable. Fluoroscopic simulation is regarded as a reasonable alternative. Common EBRT field arrangements, AP/PA and PA alone, are considered appropriate. Posterior oblique treatment is also an appropriate alternative if the kidneys can be spared, as it is an easy, relatively conformal dosimetric approach that can spare the skin if spinal surgery ever comes into play in later course of disease. The treating physician will need to judge the risk and benefit of each technique on each individual patient. However, more sophisticated highly conformal approaches like SBRT, IMRT, and protons are considered not necessary. Low- to moderate-dose steroids are often used during the course of radiation to vertebral metastases in the absence of spinal cord involvement (see Variant 2 above).

Variant 3 Discussion

This patient presents with epidural spinal cord compression at T7 and is without a history of prior therapy for his multiple myeloma. The main goals of treatment are to decompress the spinal cord and to control the pain. High- to moderate-dose steroid therapy should be started promptly to decrease cord edema/inflammation and act therapeutically against myeloma. Since plasma cell tumors are very radiosensitive even to a low to moderate dose of radiation, the recommended treatment is emergent EBRT. Adding OI to the treatment of multiple myeloma reduces pathologic vertebral fractures, SREs, and pain, and it can be considered in conjunction with EBRT. In light of the slight risk of jaw osteonecrosis associated with OI administration, a pretreatment dental evaluation to assess dentition and potential risk prior to OI use might be necessary. OI with pamidronate or zoledronic acid are U.S. Food and Drug Administration (FDA) approved for use in multiple myeloma, but not denosumab. Surgical intervention is generally not required unless present or impending spinal instability is contributing to the cord compression. Kyphoplasty procedures may be considered for pathologic vertebral compression fractures but are not indicated in the setting of spinal cord compression. Radiopharmaceuticals are used in multiple myeloma clinical trials, in association with stem cell transplantation. The presence of systemic disease coupled with his reasonably good performance status suggests that systemic treatment should be considered.

While there are no definitive data to suggest the most appropriate RT dose, fractionation schedules ranging from a single 8 Gy fraction to 40 Gy in 20 fractions are all considered appropriate. Given the fact that the patient is relatively young and has good performance status, the life expectancy can be estimated in years. For this reason, more fractionated regimens, such as 30 Gy in 10 fractions, 35 Gy in 14 fractions, or 40 Gy in 20 fractions, are favored. CT simulation to accurately include the involved vertebrae and account for body habitus in EBRT dose calculation is most desirable. Fluoroscopic simulation is regarded as a reasonable alternative. Common EBRT field arrangements, AP/PA, PA alone, and posterior obliques are considered appropriate. Posterior oblique treatment approach is favored, as it is an easy, relatively conformal dosimetric approach that can reduce the dose administered to the skin and this may be beneficial if spinal surgery comes into play in later course of disease. However, it can also result in higher lung dose. The treating physician will need to judge the risk and benefit of each technique in each individual patient. More sophisticated highly conformal approaches like SBRT, IMRT, and protons are considered insufficiently studied and therefore unjustified. Furthermore, multiple myeloma is very radiosensitive, rendering radiation dose escalation using advanced technology unnecessary for palliation of pain and spinal cord compression (see Variant 3 above).

Variant 4 Discussion

The patient's systemic tumor burden appears stable, and his only symptomatic site is that of the T7 lesion. The case raises the issue of reirradiation of the spine. Reirradiation using EBRT poses an increased risk of radiation myelitis should the patient's lifespan exceed 6 months. Means to treat this symptomatic T7 lesion include surgery, reirradiating, or systemic anticancer interventions with chemotherapy or radiopharmaceuticals. Steroids, OI, and analgesics may improve pain control and should be used. Surgery may be considered if the adjacent, irradiated bone appears stable and the patient's life expectancy is >3 to 6 months. The decision to proceed with surgery in this situation is very nuanced; patients with vertebral body compression fracture alone without significant mechanical instability are often helped with vertebral augmentation procedures such as kyphoplasty or vertebroplasty. Patients with involvement of the vertebral body and posterior elements, other evidence of spinal instability, or refractory symptoms may benefit from surgical intervention if their performance status allows. There is little information to provide guidance on reirradiation of spinal metastases. Goals of treatment include obtaining pain relief while minimizing the risk of radiation myelitis. Highly conformal techniques like proton therapy, SBRT, or IMRT can be considered if they are available and if sustained positioning is achievable for the patient. Ideally, the patient can enroll in a clinical trial, if one is available. Different fractionation regimens have been used in SBRT for reirradiation of recurrent spinal metastasis, and they are all deemed appropriate provided the cord tolerance can be respected. Surgery can provide rapid relief of debilitating pain and may be considered given the patient's good performance status. Since there is no spinal canal involvement in this case, systemic therapies, including radiopharmaceuticals could be given either as an adjuvant or alone if surgery is not a practical approach. Third line chemotherapy with erlotinib may be considered for individuals who have a good performance status and who have not had prior exposure to erlotinib or gefitinib. There is insufficient data addressing use of additional cytotoxic drugs; considerations may be given to clinical trials and best supportive care (see Variant 4 above).

Variant 5 Discussion

This patient has a good performance status, a relatively long life expectancy, and a solitary site of painful metastasis in a vertebra without canal involvement. This clinical scenario qualifies as a case of oligometastasis. The optimal management of oligometastases is an active area of research. Investigations of site-specific localized therapy compared to a more systemic approach with or without localized therapy are ongoing. Some have argued that patients with minimal sites of bone-only metastatic disease (deemed "oligometastatic") may be treated with curative intent, though the data to confirm that stance are still limited. The use of HT and OI, with or without sequential EBRT, is regarded as one of the reasonable treatment options. For this ER positive/PR positive tumor, where there is no visceral involvement, a localized therapy may be considered, ideally as part of a clinical trial. Systemic therapy is typically administered due to the likelihood of systemic involvement. Surgical intervention is regarded as less appropriate given the absence of spinal cord compression or spinal instability and alternative methods of providing site-specific disease control. Systemic radiopharmaceuticals are regarded as the least appropriate and have not been formally studied in the setting of newly diagnosed oligometastatic disease.

If EBRT is not administered to the spine at this time, then very close monitoring of the patient would be required to monitor for pain, and for early symptoms of spinal cord compression. Since this patient's survival is likely to be measured in years, hospice placement is deemed an inappropriate option.

The RT dose fractionation prescribed varies from those for long bones. Fractionation schedules ranging from a single 8 Gy fraction to 40 Gy in 20 fractions are all considered appropriate. CT simulation to accurately include the involved vertebrae and account for body habitus in EBRT dose calculation is most desirable. Fluoroscopic simulation is regarded as a reasonable alternative. Common EBRT field arrangements, AP/PA and PA alone, are considered appropriate. Posterior oblique treatment is favored as it is an easy, relatively conformal dosimetric approach that can reduce the skin dose and this may be beneficial if spinal surgery comes into play in later course of disease. However, it can also result in higher lung dose. The treating physician will need to judge the risk and benefit of each technique in each individual patient. In this setting of spinal oligometastasis and the absence of extraspinal metastasis, if aggressive local therapy is part of the treatment regimen, SBRT or IMRT aimed at delivering a higher

biologically effective dose to improve local control may be considered appropriate, particularly as part of a clinical trial. The relatively limited availability and much higher cost render proton beam therapy not appropriate (see Variant 5 above).

Variant 6 Discussion

This patient has a good performance status and a single site of painful and progressive metastasis in a vertebra without canal involvement. Standard analgesics should be used for initial pain control. Renal cell carcinoma is regarded as radioresistant histology and may not be as responsive to EBRT in the palliative dose range, although some palliative response has been observed. The use of EBRT with sequential systemic therapy with or without OI is deemed appropriate. Surgical intervention is not routinely offered in the absence of spinal cord compression or spinal instability. Systemic radiopharmaceuticals are regarded as the least appropriate.

Especially in this symptomatic spine lesion where disease progression under systemic therapy alone could incur the risk of spinal cord compression, the benefit of adding EBRT to systemic therapy in a sequential fashion is again emphasized. If EBRT is not administered to the spine, then very close monitoring of the patient would be required to assess for pain, and for early symptoms of spinal cord compression.

Given the radioresistant nature of renal cell carcinoma, a more aggressive dose regimen is deemed appropriate. If SBRT is available, it is best used in a clinical trial setting. SBRT regimens using 1 to 5 fractions are deemed appropriate. This should be combined with systemic therapy sequentially because the systemic disease still needs to be addressed. Fractionation schedules delivering a higher dose, such as 30 Gy in 10 fractions, 35 Gy in 14 fractions, or 40 Gy in 20 fractions, are deemed appropriate. SBRT dose regimens include 16 to 24 Gy in 1 fraction, 24 to 27 Gy in 3 fractions, and 30 Gy in 5 fractions, and they are all regarded as appropriate provided that spinal cord tolerance is respected. CT simulation is required to accurately include the involved vertebrae and account for body habitus in SBRT dose calculation. CT simulation is also desirable if EBRT is used. Fluoroscopic simulation is regarded as a reasonable alternative. Common EBRT field arrangements, AP/PA and PA alone, are considered appropriate. A posterior oblique treatment approach is most favored as it is an easy, relatively conformal dosimetric approach that can reduce the volume of the RT dose administered to the esophagus within the EBRT field. The relatively limited availability renders proton beam therapy not practical (see Variant 6 above).

Summary

- EBRT successfully provides rapid palliative relief from painful spinal bone metastases in the majority of cases.
- The acute side effects of palliative EBRT are usually minimal and self-limiting, while long-term side effects are uncommon and often irrelevant in a patient group with limited life expectancy.
- In good performance status patients with epidural spinal cord compression, surgical decompression should be considered, and this should be followed by EBRT if no EBRT has been given before in the same area.
- Prospective randomized trials have proven that equivalent pain relief can be achieved with varied fractionation schemes including a single 8 Gy, 20 Gy in 5 fractions, 24 Gy in 6 fractions, or 30 Gy in 10 fractions. Prolonged courses are associated with a lower incidence of retreatment, while shorter courses maximize patient and caregiver convenience.
- Reirradiation of spinal metastasis may be achieved using highly conformal techniques such as SBRT, IMRT, and proton beam therapy, although retreatment can carry a higher risk of radiation myelitis. Ideally, if there is a clinical trial available, patients should be enrolled to be treated on protocol. Surgical intervention should be considered in patients with previously irradiated spinal metastases causing severe pain or spinal compression.
- Highly conformal techniques such as SBRT, IMRT, and proton beam therapy for spinal cord compression are best tested in a clinical trial setting.
- There may be a potential survival benefit to aggressive local therapy of oligometastasis but more data is needed to better define the role of highly conformal RT techniques that allow for radiation dose escalation in this type of clinical scenario.
- Other treatments such as analgesics, including narcotic analgesics and steroids should be used initially for pain control in most cases.
- OI can be incorporated into palliative care of skeletal complications from spinal metastasis.
- Management of metastatic bone disease is palliative. A multidisciplinary team of care providers should be available to the patient, including the palliative care team. Goals of care should be defined with the patient. Hospice referral should be considered if the patient's life expectancy is ≤6 months.

Abbreviations

- CEA, carcinoembryonic antigen
- CT, computed tomography
- EBRT, external beam radiation therapy
- ER, estrogen receptor
- HER2, human epidermal growth factor receptor 2

- HT, hormonal therapy
- IMRT, intensity-modulated radiation therapy
- KPS, Karnofsky Performance Status
- MRI, magnetic resonance imaging
- OI, osteoclast inhibitors
- PR, progesterone receptor
- RT, radiation therapy
- SBRT, stereotactic body radiation therapy

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Spinal bone metastases

Guideline Category

Risk Assessment

Treatment

Clinical Specialty

Oncology

Radiation Oncology

Radiology

Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of radiologic procedures for treatment of spinal bone metastases

Target Population

Patients with spinal bone metastases

Interventions and Practices Considered

1. Surgical intervention
2. Hormonal therapy (HT)
3. External beam radiation therapy (EBRT)
4. Stereotactic body radiation therapy (SBRT)
5. Proton beam therapy
6. Intensity-modulated radiation therapy (IMRT)
7. Chemotherapy
8. Steroid therapy
9. Systemic radiopharmaceuticals
10. Osteoclast inhibitors
11. Combination therapies
12. Hospice placement
13. Observation
14. Radiation therapy dosing and treatment planning

Major Outcomes Considered

- Quality of life
- Improvement in pain control
- Survival
- Adverse effects of treatment

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches:

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 5 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Strength of Evidence Key

Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis, and results.

Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.

Category 3 - The conclusions of the study may be valid, but the evidence supporting the conclusions is inconclusive or equivocal.

Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence for all articles included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member forms his/her own opinion based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Modified Delphi Technique

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distributes surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The ratings are a scale between 1 and 9, which is further divided into three categories: 1, 2, or 3 is defined as "usually not appropriate"; 4, 5, or 6 is defined as "may be appropriate"; and 7, 8, or 9 is defined as "usually appropriate." Each panel member assigns one rating for each procedure per survey round. The surveys are collected and the results are tabulated, de-identified and redistributed after each round. A maximum of three rounds are conducted. The modified Delphi technique

enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive bias from fellow panelists in a simple, standardized and economical process.

Consensus among the panel members must be achieved to determine the final rating for each procedure. Consensus is defined as eighty percent (80%) agreement within a rating category. The final rating is determined by the median of all the ratings once consensus has been reached. Up to three rating rounds are conducted to achieve consensus.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is accepted as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Selection of appropriate radiologic treatments for patients with spinal bone metastases

Potential Harms

- Osteoclast inhibitor (OI) administration is associated with a slight risk of jaw osteonecrosis.
- Reirradiation using external beam radiotherapy (EBRT) poses an increased risk of radiation myelitis should the patient's lifespan exceed 6 months.
- The acute side effects of palliative EBRT are usually minimal and self-limiting, while long-term side effects are uncommon and often irrelevant in a patient group with limited life expectancy.

Qualifying Statements

Qualifying Statements

Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Lo SS, Lutz ST, Chang EL, Galanopoulos N, Howell DD, Kim EY, Konski AA, Pandit-Taskar ND, Rose PS, Ryu S, Silverman LN, Sloan AE, Van Poznak C, Expert Panel on Radiation Oncology-Bone Metastases. ACR Appropriateness CriteriaÂ® spinal bone metastases. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 13 p. [37 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1996 (revised 2012)

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology–Bone Metastases

Composition of Group That Authored the Guideline

Panel Members: Simon Shek-Man Lo, MB, ChB (*Principal Author and Panel Vice-chair*); Stephen T. Lutz, MD, MS (*Panel Chair*); Eric L. Chang, MD; Nicholas Galanopoulos, MD; David D. Howell, MD; Edward Y. Kim, MD; Andre A. Konski, MD; Neeta D. Pandit-Taskar, MD; Peter S. Rose, MD; Samuel Ryu, MD; Larry N. Silverman, MD; Andrew E. Sloan, MD; Catherine Van Poznak, MD

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Janjan NA, Lutz ST, Bedwinek JM, Hartsell WF, Ng A, Pieters RS Jr, Ratanatharathorn V, Silberstein EB, Taub RJ, Yasko AW, Expert Panel on Radiation Oncology--Bone Metastases. ACR Appropriateness Criteria® bone metastasis. [online publication]. Reston (VA): American College of Radiology (ACR); 2008. 26 p.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2 p. Available from the American College of Radiology (ACR) Web site .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 1 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .

- ACR Appropriateness Criteria® spinal bone metastases. Evidence table. Reston (VA): American College of Radiology; 2012. 24 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This summary was completed by ECRI on March 25, 1999. The information was verified by the guideline developer on September 9, 1999. The summary was updated on February 12, 2002. The information was verified again by the guideline developer on March 25, 2002. This NGC summary was updated by ECRI most recently on November 12, 2004. The information was verified by the guideline developer on December 21, 2004. This NGC summary was updated by ECRI Institute on August 13, 2009 and on May 22, 2013.

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